REMARKS

Applicants previously canceled Claims 13, 14, 16, 17, 25, 37, 41, and 43. Applicants have canceled Claims 29-35 herein, as being drawn to a non-elected invention, and Applicants reserve the right to pursue the subject matter of these claims in one or more divisional applications. Applicants also have canceled Claims 11, 12, 15, 19, 26, 39, and 53, and have amended Claims 1, 18, 27, 36, 40, and 42 for clarity herein. Enabling support for the amendments can be found in the application as filed (*See, e.g.*, original claims; Col. 2, para. [0012], and [0017]-[0018]; and Examples 3, 5, 6, 8, 9, 15, and 16). Therefore, no new matter is contained in the amendments. Reconsideration of the present application and allowance of pending Claims 36, 38-40, 42, 44, and 45 are respectfully requested in view of the amendments and following remarks.

Applicants also have withdrawn Claims 1-10, 18, 20, 24, 27, and 28 herein, as being drawn to non-elected inventions. Applicants note that the claims of Group II (Claims 36, 38, 40, 42, and 44-52) and Group I (Claims 1-10, 18, 20, and 24) are related as product and process of making the product, respectively. In addition, the claims of Group II (Claims 36, 38, 40, 42, and 44-52) and Group III (Claims 27 and 28) are related as product and method of using the product, respectively. Accordingly, as the product claims are believed to be in condition for allowance, Applicants request rejoinder of Claims 1-10, 18, 20, 24, 27, and 28, directed to the non-elected inventions. MPEP § 821.04(b). In addition, Applicants elected the species of GABAnergic neurons. As the claims are believed to be in condition for allowance as they relate to the elected species, Applicants request that the Patent Office examine the claims as they relate to the non-elected species which are written in dependent form or otherwise include all of the limitations of the allowable generic claim as provided by 37 C.F.R. § 1.141. Consideration and allowance of Claims 1-10, 18, 20, 24, 27, and 28 are respectfully requested.

I. Restriction Requirement

The Office Action made final the previous restriction requirement. Accordingly, Applicants have canceled Claims 11, 12, 15, 19, 29-35 and have withdrawn Claims 1-10, 18, 20, 24, 27, and 28 herein, as being drawn to non-elected inventions or species. Applicants reserve

the right to prosecute the subject matter of the canceled claims in one or more continuation or divisional applications. In addition, as noted above, because the claims of Group II (Claims 36, 38, 40, 42, and 44-52, related to a product) are believed to be in condition for allowance, Applicants respectfully request rejoinder of Claims 1-10, 18, 20, and 24 (Group II, related to processes for making the product of Group I) and Claims 27 and 28 (Group III, related to methods for using the product of Group I).

In addition, Applicants elected the species of GABAnergic neurons. As the claims are believed to be in condition for allowance as they relate to the elected species, Applicants respectfully request that the Patent Office examine the pending claims as they relate to the non-elected species at this time.

II. Rejection under 35 U.S.C. § 112, second paragraph

Claims 40, 42, 44, 45, and 53 were rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. In particular, the Office Action alleged that the description in the specification at paragraph [0023] is inconsistent with the description in the claims because the specification states that *neural progenitor cells* express nestin or vimentin, while Claim 40 states that *neural cells* derived *in vitro* from pluripotent cells express one or more detectable markers for nestin or vimentin. Applicants respectfully submit that the pending claims particularly point out and distinctly claim the subject matter of the invention.

The specification teaches that the group of cell types or species encompassed by the term "neural cells" includes the subgroup "neural progenitor cells." For example, the specification states "The invention provides a composition comprising a culture of neural cells, wherein the neural cells are preferably neural progenitor cells." Col. 3, para. [0023]. In addition, the term "neural cells" also includes the subgroups of differentiated and partially differentiated cells derived from a pluripotent or multipotent cell. *See, e.g.*, Col. 3, para. [0023]-[0025]. The specification teaches that several of the cell types encompassed by the term "neural cells," in addition to neural progenitor cells, express nestin. For example, the specification teaches in

Examples 5 and 6 that nestin is expressed on neural progenitor cells, semi-differentiated neurons, and presumptive glial cells.

> Staining of the structured essentially serum free embryoid bodies with anti-Nestin, anti-Sox1, and anti-Map2 further demonstrated the presence of multiple neural cell types: neural progenitors ($Nestin^+/Sox1^+$), and/or semi-differentiated neurons ($Nestin^+/Sox1^+$/radial $Map2^+$), differentiated neurons ($Map2^+$), and presumptive glial cells ($Nestin^+$).

Col. 16, para. [0127]; *see also* Fig. 6 and Col. 17, para. [0138] ("Immunocytochemical staining demonstrated that neural progenitors ($Nestin^+/Sox1^+$), and/or semi-differentiated neurons ($Nestin^+/Sox1^+$/radial $Map2^+$), differentiated neurons ($Map2^+$), and presumptive glial cells ($Nestin^+$) were present in these cultures and corresponded to morphological observations of these cell types."). Moreover, Example 20 further describes the identification of neural cells (*i.e.*, neural progenitor cells, semi-differentiated cells, and differentiated cells) through the detection of nestin and vimentin expression. *See* Col. 24-25. Further, the term "neural cell" is defined in the specification as being a cell that is "at least more differentiated towards a neural cell type than the pluripotent cell from which it is derived." Col. 8, para. [0069].

The currently pending claims particularly point out and distinctly claim the subject matter of the invention. Therefore, the rejection under 35 U.S.C. § 112, second paragraph should be withdrawn.

III. Rejections under 35 U.S.C. § 102

A. The Office Action rejected Claims 26, 40, 42, 44, 45, and 53 under 35 U.S.C. § 102(a) as allegedly being anticipated by Carpenter *et al.* (2001, Exp. Neurol. 172:383-97). In particular, the Office Action asserted that Carpenter *et al.* teach a cell culture composition comprising a population of human cells, expressing nestin, and differentiated into cells of a neural lineage, preferably a GABAnergic neuron. Accordingly, the Office Action concluded that Carpenter *et al.* anticipate the present invention. This rejection is moot with respect to Claims 26 and 53 as these claims have been canceled herein without prejudice or disclaimer. Applicants respectfully submit that the currently pending claims are novel over the teachings of Carpenter *et al.*

A claim is anticipated only when a single prior art reference expressly or inherently teaches each and every feature of the claim. *See Verdegaal Bros. v. Union Oil Co. of Cal.*, 814 F.2d 628 (Fed. Cir. 1987). Carpenter *et al.* do *not* teach each and every feature of the presently claimed invention. Claims 40, 42, 44, and 45 are directed to a "neural cell culture composition comprising a *predominantly homogeneous* population of human neural cells derived *in vitro* from human embryonic stem cells," wherein the cells express one or more detectable markers for nestin or vimentin, and the cells have the capacity to differentiate into neurons, oligodendrocytes, and astrocytes. Carpenter *et al.* do not teach a predominantly homogeneous population of neural cells, but rather Carpenter *et al.* teach a mixed population of cells. For example, the culture methods of Carpenter *et al.* resulted in some nestin-positive neural precursor cells, but only a subset (of undisclosed size) of the nestin-positive cells also express other neural progenitor markers such as PS-NCAM and A2B5, but not markers for mature cells. *See, e.g.*, page 388, second column, last paragraph to page 390, first column; Figure 2. Therefore, the neural cell cultures disclosed by Carpenter *et al.* clearly are not predominantly homogeneous populations of neural cells.

In addition, after magnetic bead sorting to enrich for A2B5-positive or PS-NCAM-positive cells, the enriched population was only able to differentiate a small percentage of the cells into mature cells of a neural cell lineage (*i.e.*, approximately 25-35% of the cells cultured under their differentiation conditions expressed markers for mature cells, such as MAP-2 and TH). *See* page 391, second column, last paragraph to page 392, first column. By contrast, under the disclosed conditions, the neural cell culture compositions disclosed in the present application are able to differentiate into mature cells of a neural lineage at a much higher efficiency (*i.e.*, nearly 90% differentiate into mature cells of neural lineage as indicated by TH expression). *See, e.g.*, Example 9.

Moreover, Carpenter *et al.* do not teach cells have the capacity to differentiate into neurons, oligodendrocytes, and astrocytes. Rather, cells described by Carpenter *et al.* are only able to differentiate mainly into neurons, with a very small group differentiating into GFAP positive astrocytes. For example, when using their differentiation protocol on A2B5-immunoselected neural progenitor cells, Carpenter *et al.* were only able to obtain cultures with

approximately 0.73 ± 0.6% cells expressing GFAP (*i.e.*, astrocytes) (*See* page 392, first column). Carpenter *et al.* discuss that their immunoselected cells appear to be a "mixed population of cells that can generate both neurons and astrocytes" (page 394, first column, last full para.). When their cell cultures were not first immunoselected, Carpenter *et al.*'s progenitor cells appeared to generate PS-NCAM positive cells that were mainly neuronal cells, and no GFAP positive cells (page 389, first column, bridging paragraph). Similarly, Carpenter *et al.* generated A2B5 positive cells that were mainly neurons, and "considerably less abundant" astrocytes (pages 389-90, bridging paragraph and first full paragraph). By contrast, the instant specification teaches repeatedly that the described neural cells differentiate into neurons, astrocytes, and oligodendrocytes. For example, in Example 3 (Col. 13, para. [0101]), the specification states:

> Marker analysis revealed that there were large numbers of GFAP positive astrocyte lineage cells, moderate numbers of NF200 positive neurons, and low levels of 04 positive oligodendrocytes. The seeded spheres were therefore capable of producing cells of all three neural lineages after three passages at clonal cell densities and therefore provide evidence of self-renewal and multi-potency.

See also Example 15, Col. 23, para. [0188]; Example 16, Col. 23, para. [0192].

Carpenter *et al.* do not teach each and every feature of the presently claimed invention. Therefore, Carpenter *et al.* do not anticipate the present invention, and the rejection under 35 U.S.C. § 102(a) should be withdrawn.

B. The Office Action rejected Claims 40, 42, 44, 45, and 53 under 35 U.S.C. § 102(b) as allegedly being anticipated by Deng *et al.* (2001, Biochem. Biophys. Res. Comm. 282:148-52). In particular, the Office Action alleged that Deng et al. teach a cell culture composition comprising undifferentiated cultures of human marrow stromal cells (hMSCs), expressing vimentin. The Office Action also alleged that under certain conditions, a subset of the hMSCs differentiated into cells with a typical neural cell morphology and have the capability to differentiate into cells of a neural lineage. Accordingly, the Office Action concluded that Deng *et al.* anticipate the present invention. Applicants respectfully submit that the pending claims are novel over the teachings of Deng *et al.*

Deng *et al.* do not teach each and every feature of the presently claimed invention. As noted above, the currently pending claims are directed to a human neural cell culture composition

"derived *in vitro* from human *embryonic stem cells*" (emphasis added). By contrast, Deng *et al.* teach a cell culture composition of *hMSCs* that when cultured under certain conditions results in a small subset of the hMSCs differentiating into cells with a neuronal morphology. Deng *et al.* do not teach or suggest the use of human embryonic stem cells for producing a predominantly homogeneous population of neural cells.

Deng *et al.* do not teach each and every feature of the presently claimed invention. Accordingly, Deng *et al.* do not anticipate the present invention, and the rejection under 35 U.S.C. § 102(b) should be withdrawn.

C. The Office Action rejected Claim 26 under 35 U.S.C. § 102(a) as allegedly being anticipated by Jain *et al.* (2003, Exp. Neurol. 182:113-23). This rejection is moot as Claim 26 has been canceled herein without prejudice or disclaimer.

D. The Office Action rejected Claim 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Westmoreland *et al.* (2001, Biochem. Biophys. Res. Comm. 284:674-80). This rejection is moot as Claim 26 has been canceled herein without prejudice or disclaimer.

E. The Office Action rejected Claim 26 under 35 U.S.C. § 102(b) as allegedly being anticipated by Benagiano *et al.* (2000, Histochem. Cell Biol. 114:191-95). This rejection is moot as Claim 26 has been canceled herein without prejudice or disclaimer.

IV. Double Patenting

Claims 26, 40, 42, 44, 45, and 53 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting over Claims 46-52 of copending Application No. 10/539,951. This rejection is moot with respect to Claims 26 and 53 as these claims have been canceled herein without prejudice or disclaimer. Applicants respectfully submit that this is a provisional rejection, and therefore, Applicants will respond to this rejection upon the withdrawal of all other rejections in this application or the copending Application No. 10/539,951.

CONCLUSION

Applicants believe that the present application, as amended, is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The foregoing is submitted as a full and complete response to the Office Action mailed July 2, 2007.

A petition for a three-month extension of time and the required fee are submitted herewith. No additional fees are believed due at this time. However, please charge any fees that may be due, or credit any overpayment, to Deposit Account 19-5029 (Ref. No.: 18465-0036). In addition, if there are any issues that can be resolved by a telephone conference or an Examiner's amendment, the Examiner is invited and encouraged to call the undersigned attorney at (404) 853-8000.

Respectfully submitted,

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